

REMARKS

Claims 4 and 6 have been amended to correct typographical errors. Claim 7 has been canceled. Claim 8 has been amended to correct a typographical error and to more clearly define the nucleoside 5'-triphosphate of claims 1 and 3. No new matter has been added. Thus, entry of the Amendment is respectfully requested.

Claims 6-8 have been rejected under 35 U.S.C. §112, second paragraph, as failing to further limit the identity of the compounds claimed.

Applicants submit that claim 6 further defines the removable blocking moiety of the nucleoside 5'-triphosphate of claims 1 or 3 as being "enzymatically removable." This recitation further defines the removable blocking moiety and therefore distinguishes the nucleoside 5'-triphosphate of claims 1 or 3. Claim 7 has been cancelled without prejudice. Claim 8 has been amended to recite that the nucleoside 5'-triphosphate is "linked to a solid support via said removable blocking moiety." Clearly, Applicants are claiming a structure rather than a subsequent process step. Accordingly, reconsideration and withdrawal of this ground of rejection are requested.

Claims 1, 3 and 4 have been rejected under 35 U.S.C. § 103 as obvious over each of *Buhr et al.* (U.S. Patent No. 5,466,786) and *Inoue et al.* (U.S. Patent No. 4,965,350). The Examiner contends that *Buhr* discloses 2'-modified 5'-triphosphates that in the 3'-position may be a phosphate moiety selected from the ester PO_3^{-2} , and potential hydrocarbyl moieties, which contain heteroatoms and alkyl chains such as $\text{P}(\text{O})\text{NR}_2$, $\text{P}(\text{O})\text{R}$, $\text{P}(\text{O})\text{OR}'$, CO and CNR_2 , wherein R is H or alkyl (1-6 C) and R' is alkyl (1-6 C). The Examiner concludes, therefore, that *Buhr* renders the claimed compounds, which are 5'-triphosphate compounds with hydrocarbyl, ester and phosphate moieties suitable in the 3'-position, obvious to those skilled in the art. The Examiner also contends that *Inoue* discloses nucleotide compounds wherein the 5'-position may be substituted with a moiety "which is not only a phosphate, but also an ester." The Examiner alleges that the difference between the compounds disclosed in *Inoue* and the instantly claimed compounds is the limited display of variability in the 3'-position as disclosed in *Inoue*. The Examiner concludes, therefore, that it would have been obvious to obtain a 5'-triphosphate

nucleoside compound with an ester, phosphate or hydrocarbyl moiety in the 3'-position, because the prior art teaches these monomers for use in the preparation of oligomers.

Applicants respectfully traverse the rejection, because the teachings of *Buhr* and *Inoue* would not have rendered obvious the claimed compounds. *Buhr* teaches 2' modified oligonucleotides which are capable of being used in drug delivery systems or for interference with nucleic acid activity. *Buhr* fails to teach or suggest, however, that the moieties in the 3' position of the compounds disclosed therein are capable of being removed. In fact, *Buhr* discloses that the 3' moieties $P(O)NR_2$, $P(O)R$, $P(O)OR'$, CO and CNR_2 , which the Examiner has referenced, are used as linking groups in intermediate compounds -- not blocking moieties. The only protecting groups disclosed in *Buhr* are those typically used in the chemical synthesis of oligomers (e.g., 4, 4'-dimethoxy trityl (DMT), 4-monothoxytrityl and trityl). (See col. 4, lns. 47-53.) Thus, there is no teaching or suggestion in *Buhr* of the nucleoside 5'-triphosphates having blocking moieties claimed by Applicants.

Similarly, there is no teaching in *Inoue* that the 3'-position moieties disclosed therein are or can be used as removable blocking moieties as required by Applicants' claimed invention. Instead, *Inoue* discloses fluorescent pyrimidine nucleotide derivatives which may be introduced into DNA oligomers or polymers by two methods, namely organic or enzymatic synthesis. With respect to the enzymatic synthesis of the compounds disclosed therein, the first method discussed, nick translation, is a template-dependent method which does not require the use of 5'-triphosphates having removable blocking moieties. The second method, homopolymeric tailing with terminal deoxynucleotidyl transferase, also does not discuss the use of nor does it require removable blocking moieties.

In light of the above, *Buhr* and *Inoue* do not provide a disclosure which renders obvious the presently claimed invention. These patents fail to disclose the use of a removable blocking group at the 3'-carbon of a nucleoside 5'-triphosphate as required by the claims. Because *Buhr* and *Inoue* failed to teach or suggest the nucleoside 5'-triphosphates blocked at the 3'-position with the removable moieties of Claims 1 and 3, or the advantages obtained therefrom, the pending claims are patentably distinguishable over the cited references. Reconsideration and withdrawal of this rejection are therefore respectfully requested.

Applicants submit that the present amendment and accompanying remarks serve to overcome all outstanding rejections and place all pending claims in condition for immediate allowance. An early Notice to this effect is earnestly solicited. The Examiner is encouraged to contact the undersigned if he has any remaining questions.

Respectfully submitted,

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